
Animal models of pulmonary hypertension: Rho kinase inhibition.

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Public Summary:

Pulmonary Hypertension is a terminology encompassing a range of etiologically different pulmonary vascular diseases. The most common is that termed pulmonary arterial hypertension or PAH; a rare but often fatal disease characterized by a mean pulmonary arterial pressure of >25 mmHg. PAH is associated with a complex etiology highlighted by core characteristics of increased pulmonary vascular resistance and elevation of mean pulmonary artery pressure. When sustained, pulmonary vascular remodeling occurs and eventually patients pass away due to right heart failure. Hypoxic pulmonary vasoconstriction is an early event occurring in pulmonary hypertension due to chronic exposure to hypoxia. While the underlying mechanisms of hypoxic pulmonary vasoconstriction may be controversial, a role for RhoA/Rho kinase mediated regulation of intracellular Ca^{2+} has been recently identified. Further study suggests that RhoA may have an integral role in other pathophysiological processes such as cell proliferation and migration occurring in all forms of PH. Indeed Rho proteins are known to play essential roles in actin cytoskeleton organization in all eukaryotic cells and thus Rho and Rho-GTPases are implicated in fundamental cellular processes such as cellular proliferation, migration, adhesion, apoptosis and gene expression. This review focuses on providing an overview of the role of RhoA/Rho kinase in currently available animal models of pulmonary hypertension.

Scientific Abstract:

Pulmonary Hypertension is a terminology encompassing a range of etiologically different pulmonary vascular diseases. The most common is that termed pulmonary arterial hypertension or PAH; a rare but often fatal disease characterized by a mean pulmonary arterial pressure of >25 mmHg. PAH is associated with a complex etiology highlighted by core characteristics of increased pulmonary vascular resistance and elevation of mean pulmonary artery pressure. When sustained, pulmonary vascular remodeling occurs and eventually patients pass away due to right heart failure. Hypoxic pulmonary vasoconstriction is an early event occurring in pulmonary hypertension due to chronic exposure to hypoxia. While the underlying mechanisms of hypoxic pulmonary vasoconstriction may be controversial, a role for RhoA/Rho kinase mediated regulation of intracellular Ca^{2+} has been recently identified. Further study suggests that RhoA may have an integral role in other pathophysiological processes such as cell proliferation and migration occurring in all forms of PH. Indeed Rho proteins are known to play essential roles in actin cytoskeleton organization in all eukaryotic cells and thus Rho and Rho-GTPases are implicated in fundamental cellular processes such as cellular proliferation, migration, adhesion, apoptosis and gene expression. This review focuses on providing an overview of the role of RhoA/Rho kinase in currently available animal models of pulmonary hypertension.

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